

**Form PTO-1449 Modified**

Docket No.  
**ISIS-3013**

Serial No.  
**09/403,539**

List of Patent and Publications  
Cited by Applicant  
(Use several sheets if necessary)

Applicant  
**Nicholas M. Dean et al.**

U.S. Department of Commerce  
Patent and Trademark Office

Filing Date  
**January 4, 2000**

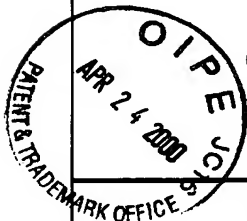
Group  
**Not Yet Assigned**

**OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)**

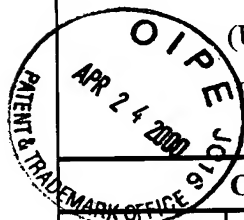
mg	AA	Agrawal et al. (eds.), "Methods of Molecular Biology", in <i>Protocols for Oligonucleotide Conjugates</i> , Agrawal, S. (ed.), Humana Press, New Jersey, <b>1994</b> , Vol. 26, 1-72
mg	AB	Agrawal, S. et al., "Pharmacokinetics, biodistribution, and stability of oligodeoxynucleotide phosphorothioates in mice", <i>Proc. Natl. Acad. Sci.</i> , <b>1991</b> , 88, 7595-7599
mg	AC	Albert, P.R. et al., "Antisense knockouts: molecular scalpels for the dissection of signal transduction", <i>Trends Pharmacol. Sci.</i> , <b>1994</b> , 15, 250-254
mg	AD	Benet, L.Z. et al., "Pharmacokinetics: The Dynamics of Drug Absorption, Distribution, and Elimination", <i>Goodman &amp; Gilman's The Pharmacological Basis of Therapeutics</i> , 9th Ed., Hardman et al. (eds.), McGraw-Hill, New York, NY, <b>1996</b> , Chapter 1, 3-9
mg	AE	Berge, S.M. et al., "Pharmaceutical Salts", <i>J. Pharm. Sci.</i> , <b>1977</b> , 66, 1-19
mg	AF	Block, L., "Medicated Applications", <i>Remington's Pharmaceutical Sciences</i> , 18th Ed., Gennaro (ed.), Mack Publishing Co., Easton, PA, <b>1990</b> , Ch. 87, 1596-1614
mg	AG	Brunton, L.L., "Agents Affecting Gastrointestinal Water Flux and motility; Emesis and-Antiemetics; Bile Acids and Pancreatic Enzymes", <i>Goodman &amp; Gilman's The Pharmacological Basis of Therapeutics</i> , 9th Ed., Hardman et al. (Eds.), McGraw-Hill, New York, <b>1996</b> , Chapter 38, 934-935
mg	AH	Buur, A. et al., "Penetration of 5-Fluorouracil and prodrugs across the intestine of the albino rabbit: Evidence for shift in absorption site from the upper to the lower region of the gastrointestinal tract by prodrugs", <i>J. Controlled Release</i> , <b>1990</b> , 14, 43-51
mg	AI	Chonn, A. et al., "Recent advances in liposomal drug-delivery systems", <i>Curr. Opin. Biotechnology</i> , <b>1995</b> , 6, 698-708
mg	AJ	Crooke, S.T. et al., "Progress in the development and patenting of antisense drug discovery technology", <i>Exp. Opin. Ther. Patents</i> , <b>1996</b> , 6, 855-870
mg	AK	Crooke, S.T. et al., "Pharmacokinetic Properties of Several Novel Oligonucleotide Analogs in mice", <i>J. Pharmacol. Exp. Therapeutics</i> , <b>1996</b> , 277, 923-937

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		Applicant <b>Nicholas M. Dean et al.</b>	
		Filing Date <b>January 4, 2000</b>	Group <b>Not Yet Assigned</b>
<b>OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)</b>			
mg	AL	Crooke, R.M., " <i>In Vitro</i> and <i>In Vivo</i> Toxicology of First Generation Analogs," in <i>Antisense Research and Applications</i> , Crooke et al. (eds.), CRC Press, Inc., Boca Raton, FL, <b>1993</b> , Chapter 27, pages 471-492	
mg	AM	Dean, N.M. et al., "Inhibition of protein kinase C- $\alpha$ expression in mice after systemic administration of phosphorothioate antisense oligodeoxynucleotides", <i>Proc. Natl. Acad. Sci.</i> , <b>1994</b> , 91, 11762-11766	
mg	AN	DiSanto, A.R., "Bioavailability and Bioequivalency Testing", <i>Remington's Pharmaceutical Sciences</i> , 18th Ed., Gennaro (ed.), Mack Publishing Co., Easton, PA, <b>1990</b> , Ch. 76, 1451-1458	
mg	AO	El-Hariri, L.M. et al., "The Mitigating Effects of Phosphatidylcholines on Bile Salt- and Lysophosphatidylcholine-induced Membrane Damage", <i>J. Pharm. Pharmacol.</i> , <b>1992</b> , 44, 651-654	
mg	AP	Geary, R.S. et al., "Characterization of Ethiofos Absorption in the Rat Small Intestine", <i>Biopharmaceutics &amp; Drug Disposition</i> , <b>1991</b> , 12, 261-274	
mg	AQ	Gebeyehu, G. et al., "Novel bitinylated nucleotide - analogs for labeling and colorimetric detection of DNA", <i>Nucl. Acids Res.</i> , <b>1987</b> , 15, 4513-4534	
mg	AR	Genetic Engineering News: "ISIS Pharmaceuticals Demonstrates Efficiency in Crohn's Disease with its Antisense Drug", March 1, <b>1997</b> , pg 1 and 34	
mg	AS	Harvey, S.C., "Drug Absorption, Action, and Disposition", <i>Remington's Pharmaceutical Sciences</i> , 18th Ed., Gennaro (ed.), Mack Publishing Co., Easton, PA, <b>1990</b> , Ch. 35, 711-715	
mg	AT	Hirahata, "Study of DDS to the Lymphnode-Metastases of the Gastric Cancer by the Endoscopic Injection of Lip-ADM," <i>Jpn. J. Cancer Chemother.</i> , <b>1992</b> , 19(10), 1591-1594 (English summary attached)	
mg	AU	Iverson, P., " <i>In Vivo</i> Studies with Phosphorothioate Oligonucleotides: Rationale for Systemic Therapy," in: <i>Antisense Research and Applications</i> , Crooke et al. (eds.), CRC Press, Inc., Boca Raton, FL, <b>1993</b> , Chapter 26, pages 461-469	
mg	AV	Iverson, P., "In Vivo studies with phosphorothioate oligonucleotides: pharmacokinetics prologue", <i>Anti-Cancer Drug Des.</i> , <b>1991</b> , 6, 531-538	
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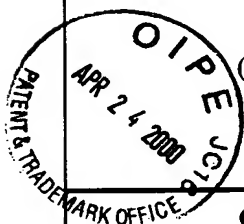


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ms	AW	Kabanov, A.V., "A new class of antivirals: antisense oligonucleotides combined with a hydrophobic substituent effectively inhibit influenza virus reproduction and synthesis of virus-specific proteins in MDCK cells", <i>FEBS Letts.</i> , <b>1990</b> , 259, 327-330
ms	AX	Katocs, A.S. et al., "Biological Testing", <i>Remington's Pharmaceutical Sciences</i> , 18th Ed., Gennaro (ed.), Mack Publishing Co., Easton, PA, <b>1990</b> , Ch. 27, 484-494
ms	AY	Kornberg, A. et al., <i>DNA Replication</i> , W.H. Freeman & Co., San Francisco, <b>1980</b> , 4-7
ms	AZ	Kornberg, A., <i>DNA Replication</i> , W.H. Freeman and Co., San Francisco, <b>1980</b> , 75-77
ms	BA	Lee, V.H.L. et al., "Mucosal Penetration Enhancers For Facilitation of Peptide and Protein Drug Absorption", <i>Crit. Rev. Ther. Drug Carrier Systems</i> , <b>1991</b> , 8, 91-192
ms	BB	Leeds, J.M. et al., "Quantitation of Phosphorothioate Oligonucleotides in Human Plasma", <i>Analyt. Biochem.</i> , <b>1996</b> , 235, 36-43
ms	BC	Letsinger, R.L. et al., "Cholesteryl-conjugated oligonucleotides: Synthesis, properties and activity as inhibitors of replication of human immunodeficiency virus in cell culture", <i>Proc. Natl. Acad. Sci.</i> , <b>1989</b> , 86, 6553-6556
ms	BD	Longer, M.A. et al., "Sustained-Release Drug Delivery Systems", <i>Remington's Pharmaceutical Sciences</i> , 18th Ed., Gennaro (ed.), Mack Publishing Co., Easton, PA, <b>1990</b> , Ch. 91, 1676-1693
ms	BE	Manoharan, M. et al., "Lipidic Nucleic Acids", <i>Tetrahedron Letts.</i> , <b>1995</b> , 36, 3651-3654
ms	BF	Manoharan M. et al., "Oligonucleotide Conjugates: Alteration of the Pharmacokinetic Properties of Antisense Agents", <i>Nucleosides and Nucleotides</i> , <b>1995</b> , 14, 969-973
ms	BG	Manoharan, M. et al., "Introduction of a Lipophilic Thioether Tether in the Minor Groove of Nucleic Acids for Antisense Applications", <i>Bioorg. Med. Chem. Letts.</i> , <b>1993</b> , 3, 2765-2770

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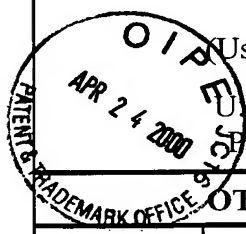
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<i>ms</i>	<b>BH</b>	Manoharan, M. et al., "Chemical Modifications to Improve Uptake and Bioavailability of Antisense Oligonucleotides", <i>Annals NY Acad. Sciences</i> , <b>1992</b> , 660, 306-309
<i>ms</i>	<b>BI</b>	Manoharan M. et al., "Cholic Acid-Oligonucleotide Conjugates for Antisense Applications", <i>Bioorganic Med. Chem. Letts.</i> , <b>1994</b> , 4, 1053-1060
<i>ms</i>	<b>BJ</b>	Martin, P., "Ein neuer Zugang zu 2'-O-Alkylribonucleosiden und Eigenschaften deren Oligonucleotide", <i>Helvetica Chemica Acta</i> , <b>1995</b> , 78, 486-504 (English summary included)
<i>ms</i>	<b>BK</b>	Mishra, R.K. et al., "Improved leishmanicidal effect of phosphorotioate antisense oligonucleotides by LDL-mediated delivery", <i>Biochim. Et Biophysica</i> , <b>1995</b> , 1264, 229-237
<i>ms</i>	<b>BL</b>	Miyao, T. et al., "Stability and Pharmacokinetic Characteristics of Oligonucleotides Modified at Terminal Linkages in Mice", <i>Antisense Res. &amp; Dev.</i> , <b>1995</b> , 5, 115-121
<i>ms</i>	<b>BM</b>	Muranishi, S., "Absorption Enhancers", <i>Crit. Rev. Ther. Drug Carrier Systems</i> , <b>1990</b> , 7, 1-33
<i>ms</i>	<b>BN</b>	Nairn, J.G., "Solutions, Emulsions, Suspensions and Extracts", <i>Remington's Pharmaceutical Sciences</i> , 18th Ed., Gennaro (ed.), Mack Publishing Co., Easton, PA, <b>1990</b> , Ch. 83, 1519-1544
<i>ms</i>	<b>BO</b>	Nielsen, P.E. et al., "Sequence-Selective Recognition of DNA by Strand Displacement with a Thymine-Substituted Polyamide", <i>Science</i> , <b>1991</b> , 254, 1497-1500
<i>ms</i>	<b>BP</b>	Nies, A.S. et al., "Principles of Therapeutics", <i>Goodman &amp; Gilman's The Pharmacological Basis of Therapeutics</i> , 9th Ed., Hardman et al. (eds.), McGraw-Hill, New York, NY, <b>1996</b> , Ch. 3, 43-62
<i>ms</i>	<b>BQ</b>	Oberhauser, B. et al., "Effective incorporation of 2'-O-methyl-oligonucleotides into liposomes and enhanced cell association through modification with thiocholesterol", <i>Nucl. Acids Res.</i> , <b>1992</b> , 20, 533-538
<i>ms</i>	<b>BR</b>	Porter, S.C., "Coating of Pharmaceutical Dosage Forms", <i>Remington's Pharmaceutical Sciences</i> , 18th Ed., Gennaro (ed.), Mack Publishing Co., Easton, PA, <b>1990</b> , Ch. 90, 1666-1675

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mez	BS	Robertson, D., "Chrohn's trial shows the pros of antisense", <i>Nature Biotech.</i> , <b>1997</b> , 15, 209
mez	BT	Rudnic, E. et al., "Oral Solid Dosage Forms", <i>Remington's Pharmaceutical Sciences</i> , 18th Ed., Gennaro (ed.), Mack Publishing Co., Easton, PA, <b>1990</b> , Ch. 89, 1633-1665
mez	BU	Saison-Behmoaras, T. et al., "Short modified antisense oligonucleotides directed against Ha-ras point mutation induce selective cleavage of the mRNA and inhibit T24 cells proliferation", <i>EMBO J.</i> , <b>1991</b> , 10, 1111-1118
mez	BV	Shea, R.G. et al., "Synthesis, hybridization properties and antiviral activity of lipid-oligodeoxynucleotide conjugates", <i>Nucl. Acids Res.</i> , <b>1990</b> , 18, 3777-3783
mez	BW	Svinarchuk, F.P. et al., "Inhibition of HIV proliferation in MT-4 cells by antisense oligonucleotide conjugated to lipophilic groups", <i>Biochimie</i> , <b>1993</b> , 79, 49-54
mez	BX	Takahashi, H. et al., "The Use of a Perfluorochemical Emulsion as a Bascular Perfusate in Drug Absorption", <i>J. Pharm. Pharmacol.</i> , <b>1988</b> , 40, 252-257
mez	BY	Takakura, Y. et al., "Uptake Characteristics of Oligonucleotides in the Isolated Rat Liver Perfusion System", <i>Antisense &amp; Nuc. Acid Drug Dev.</i> , <b>1996</b> , 6, 177-183
mez	BZ	van Berge-Henegouwen, G.P., "Pharmacology of Chenodeoxycholic Acid", <i>Gastroenterology</i> , <b>1977</b> , 73, 300-309
mez	CA	Vasseur, J.J. et al., "Oligonucleosides: Synthesis of a Novel Methylhydroxylamine-linked Nucleoside Dimer and Its Incorporation into Antisense Sequences", <i>J. Am. Chem. Soc.</i> , <b>1992</b> , 114, 4006-4007
mez	CB	Wahlestedt, C. et al., "Antisense oligodeoxynucleotides to NMDA-R1 receptor channel protect cortical neurons from excitotoxicity and reduce focal ischaemic infarctions", <i>Nature</i> , <b>1993</b> , 363, 260-263
mez	CC	Wahlestedt, C. et al., "Modulation of Anxiety and Neuropeptide Y-Y1 Receptors by Antisense Oligodeoxynucleotides", <i>Science</i> , <b>1993</b> , 259, 528-531
mez	CD	Yamashita, S. et al., "Effects of diclofenac sodium and disodium ethylenediaminetetraacetate on electrical parameters of the mucosal membrane and their relation to the permeability enhancing effects in the rat jejunum", <i>J. Pharm. Pharmacol.</i> , <b>1987</b> , 39, 621-626

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**Not Yet Assigned****U. S. PATENT DOCUMENTS**

Examiner Initial		Document No.	Date	Name	Class	Subclass
<i>my</i>	CE	4,309,404	01/05/82	DeNeale et al.	424	21
	CF	4,309,406	01/05/82	Guley et al.	424	21
	CG	4,426,330	01/17/84	Sears	260	403
	CH	4,534,899	08/13/85	Sears	260	403
	CI	4,556,552	12/03/85	Porter et al.	424	32
<i>me</i>	CJ	4,689,320	08/25/87	Kaji	514	44
<i>me</i>	CK	4,704,295	11/03/87	Porter et al.	427	3-
<i>me</i>	CL	4,806,463	02/21/89	Goodchild et al.	435	5
<i>me</i>	CM	4,835,263	05/30/89	Nguyen et al.	536	27
<i>me</i>	CN	5,004,810	04/02/91	Draper	536	27

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Examiner Initial		Document No.	Date	Country	Translation YES NO	
<i>my</i>	CO	WO 92/20823	11/26/92	PCT	X	
<i>my</i>	CP	WO 93/24510	12/09/93	PCT	X	
<i>my</i>	CQ	WO 94/26764	11/24/94	PCT	X	
<i>me</i>	CR	WO 96/20732	07/11/96	PCT	X	
<i>me</i>	CS	WO 96/32496	10/17/96	PCT	X	
<i>me</i>	CT	WO 96/34008	10/31/96	PCT	X	
<i>me</i>	CU	WO 97/05267	02/13/97	PCT	X	

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Examiner Initial		Document No.	Date	Name	Class	Subclass
<i>my</i>	CV	5,013,556	05/07/91	Woodle et al.	424	450
<i>me</i>	CW	5,034,506	07/23/91	Summerton et al.	528	391
<i>me</i>	CX	5,087,617	02/11/92	Smith	514	44
<i>me</i>	CY	5,098,890	03/24/92	Gerwirtz et al.	514	44
<i>me</i>	CZ	5,108,921	04/28/92	Low et al.	435	240.1
<i>me</i>	DA	5,135,917	08/04/92	Burch	514	44
<i>me</i>	DB	5,138,045	08/11/92	Cook et al.	536	27
<i>my</i>	DC	5,166,195	11/24/92	Ecker	514	44
<i>me</i>	DD	5,194,428	03/16/93	Agrawal et al.	514	44
<i>me</i>	DE	5,212,295	05/18/93	Cook	536	26.7
<i>me</i>	DF	5,213,804	05/25/93	Martin et al.	424	450
<i>my</i>	DG	5,218,105	06/08/93	Cook et al.	536	25.31
<i>my</i>	DH	5,227,170	07/13/93	Sullivan	424	450
<i>me</i>	DI	5,242,906	09/07/93	Pagano et al.	514	44
<i>my</i>	DJ	5,264,221	11/23/93	Tagawa et al.	424	450
<i>me</i>	DK	5,264,423	11/23/93	Cohen et al.	514	44
<i>me</i>	DL	5,276,019	01/04/94	Cohen et al.	514	44
<i>me</i>	DM	5,286,717	02/15/94	Cohen et al.	514	44
<i>me</i>	DN	5,354,844	10/11/94	Beug et al.	530	345
<i>me</i>	DO	5,356,633	10/18/94	Woodle et al.	424	450
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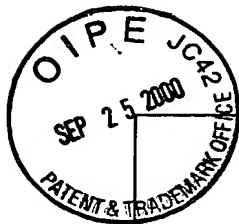
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<i>me</i>	DP	5,378,825	01/03/95	Cook et al.	536	25.34
<i>me</i>	DQ	5,386,023	01/31/95	Sanghvi et al.	536	25.3
<i>me</i>	DR	5,395,619	03/07/95	Zalipsky et al.	424	450
<i>me</i>	DS	5,416,016	05/16/95	Low et al.	435	240.1
<i>me</i>	DT	5,417,978	05/23/95	Tari et al.	424	450
<i>me</i>	DU	5,457,191	10/10/95	Cook et al.	536	27.13
<i>me</i>	DV	5,459,127	10/17/95	Felgner et al.	514	7
<i>me</i>	DW	5,459,255	10/17/95	Cook et al.	536	27.13
<i>me</i>	DX	5,462,854	10/31/95	Coassin et al.	435	6
<i>me</i>	DY	5,469,854	11/28/95	Unger et al.	128	662.02
<i>me</i>	DZ	5,506,351	04/09/96	McGee	536	55.3
<i>me</i>	EA	5,512,295	04/30/96	Kornberg et al.	424	450
<i>me</i>	EB	5,521,291	05/28/96	Curiel et al.	530	391.7
<i>me</i>	EC	5,521,302	05/28/96	Cook	536	25.31
<i>me</i>	ED	5,527,528	06/18/96	Allen et al.	424	178.1
<i>me</i>	EE	5,534,259	06/09/96	Zalipsky et al.	424	450
<i>me</i>	EF	5,534,496	07/09/96	Lee et al.	514	17
<i>me</i>	EG	5,539,082	07/23/96	Nielsen et al.	530	300
<i>me</i>	EH	5,541,307	07/30/96	Cook et al.	536	23.1
<i>me</i>	EI	5,543,152	08/06/96	Webb et al.	424	450

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<i>meg</i>	EJ	5,543,158	08/06/96	Gref et al.	424	501
<i>ME</i>	EK	5,547,932	08/20/96	Curriel et al.	435	65
<i>ME</i>	EL	5,554,746	09/10/96	Ravikumar et al.	540	200
<i>ME</i>	EM	5,556,948	09/17/96	Tagawa et al.	530	391.9 <sup>a</sup>
<i>ME</i>	EN	5,571,902	11/05/96	Ravikumar et al.	536	22.1
<i>ME</i>	EO	5,578,718	11/26/96	Cook et al.	536	27.21
<i>ME</i>	EP	5,580,575	12/03/96	Unger et al.	424	450
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<i>ME</i>	ER	5,587,361	12/24/96	Cook et al.	514	44
<i>ME</i>	ES	5,587,469	12/24/96	Cook et al.	536	23.1
<i>ME</i>	ET	5,587,470	12/24/96	Cook et al.	536	23.1
<i>ME</i>	EU	5,591,721	01/07/97	Agrawal et al.	514	44
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#6

Sheet 1 of 1

**Form PTO-1449 Modified**List of Patent and Publications  
Cited by Applicant  
(Use several sheets if necessary)U.S. Department of Commerce  
Patent and Trademark OfficeDocket No.  
**ISIS-3013**Serial No.  
**09/403,539**Applicant  
**Nicholas M. Dean, et al.**Filing Date  
**January 4, 2000**Group  
**1614****U. S. PATENT DOCUMENTS**

Examiner Initial		Document No.	Date	Name	Class	Subclass

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<i>ms</i>	AA	WO 95/02069	01/19/95	PCT		
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EXAMINER

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